Amendments to the Specification

Please amend the following paragraphs of the specification, identified by page and line number, to read as follows.

Replacement Paragraph for page 1, line 17 to line 24

As early identification of patients at risk for developing hypertensive end organ damage, such as heart failure, may prevent rapid progression, it would be preferable to be able to identify those patients in which heart failure is likely to occur before it actually does so. In ~~adddition~~ addition, it would be preferable to be able to identify those patients suffering from heart failure who are at risk for developing severe complications.

Replacement Paragraph for page 12, line 14 to line 30

Sequencing, membrane spotting, and cDNA hybridization for macroarray

Clones of the differentially expressed genes identified by microarray were obtained from Incyte genomics and sequenced with a 5'-GGTGACACTATAGAAGAGC-3' (SEQ ID NO: 1) primer (Eurogentec, Seraing, Belgium). After confirming the identity by sequencing, the plasmid inserts were amplified by a PCR reaction with 5'-ACCATGATTACGCCAAGCTC-3' (SEQ ID NO: 2) and 3'-ACGACGGCCAGTGAATTGAA-5' (SEQ ID NO: 3) primers. Each clone was then spotted in duplicate on nylon membranes (macroarray). The dot blots were scanned with a personal fx-phospho imager (Cyclone System Packard, Meriden, CO, USA). Individual ~~hybridisation~~ hybridization signals were identified and quantified densitometrically using Quantity One, Version 4.2.3 software (BioRad, Munich, Germany). Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was selected as a housekeeping gene for internal normalization of the blots.

Replacement Paragraph for page 15, line 29 to page 16, line 9

Bioinformatic analysis pointed to three novel cardiac matrix-related genes

Since no information was available as to the function of many of the overexpressed genes in HF, we subjected all the 49 genes to bioinformatic analysis. Initially, we made a broad

functional classification of the HF susceptibility genes using GeneFIND (Gene Family Identification Network Design) System (~~http://www-nbrf.georgetown.edu~~), which combines several search/alignment tools to provide rapid and accurate gene family. This strategy indicated that most of the overexpressed genes encode matrix-related proteins. Notably, the functions of 3 selected susceptibility genes (osteoactivin, thrombospondin-2 and collagen VI) were not previously reported in the myocardium.

Replacement Paragraph for page 23, line 15 to line 21

Primers and probes

Primers (forward, 5'-CCCGACTGGACCACTGACA-3' (SEQ ID NO: 4), reverse, 5'-CAGCATGCGAGGCATGACT-3' (SEQ ID NO: 5) and probe, 5'-TGCCCTACGATATGCCCTTGCCTG-3' (SEQ ID NO: 6)) specific to galectin-3 were designed from sequences available in GenBank™ using Primer Express Software (PE Applied Biosystems, Foster City, CA, USA).

Replacement Paragraph for page 24, line 1 to line 12

Sequencing, membrane spotting and cDNA hybridization for macroarray

Clones of the differentially expressed genes identified by microarray were obtained from Incyte genomics and sequenced with 5'-GGTGACACTATAGAAGAGC-3' (SEQ ID NO: 7) primer (Eurogentec, Seraing, Belgium). After confirming the identity, the plasmid inserts were amplified by PCR reaction with the 5'-ACCATGATTACGCCAAGCTC-3' (SEQ ID NO: 8) and 3'-ACGACGGCCAGTGAATTGAA-5' (SEQ ID NO: 9) primers. Each clone was then spotted in duplicates on nylon membrane (macroarray). The dot blots were scanned with the personal fx-phospho imager (Cyclone System Packard, Meriden, CO, USA).

Replacement Paragraph for page 34, line 1 to line 31

Table 1. Sequences of real-time quantitative RT-PCR primers and probes of candidate gene transcripts

Gene/primer	Sequence (5'→3')	Position	Species
Cyclophilin A (M19533)			
Fwd	GGGAGAAAGGATTTGGCTATAAGG (SEQ ID NO: 10)	167-190	Rat
Probe	TGAAGTCACCACCCTGGCACATGAAT (SEQ ID NO: 11)	219-244	
Rev	GCCACCAGTGCCATTATGG (SEQ ID NO: 12)	249-267	
Thrombospondin 2 (XM_214778)			
Fwd	GAAATGGTCTACTTCTCAGACCTCAAG (SEQ ID NO: 13)	603-629	Rat
Probe	CCCTGCTCTCTAGGCATCTCTGCACTCAT (SEQ ID NO: 14)	631-659	
Rev	GCACACTGCTGGAGCTGGA (SEQ ID NO: 15)	791-809	
Osteoactivin (NM_002510)			
Fwd	GGACTTCATTGTGACCTGCAAA (SEQ ID NO: 16)	1350-1371	Rat
Probe	CCACTCCCACGGAAGCCTGTACGAT (SEQ ID NO: 17)	1376-1400	
Rev	ACCCTGTTCTGGGCGATCT (SEQ ID NO: 18)	1421-1439	
Collagen VI (TC322135)			
Fwd	CCCTCCTTGCAGGCAGAAC (SEQ ID NO: 19)	816-834	Rat
Probe	ATGCCTTGCAGATCAATAACACAGCAGTAGG (SEQ ID NO: 20)	845-875	
Rev	CAGGAGGACCGAGAGCTCAT (SEQ ID NO: 21)	897-916	
Brain natriuretic peptide (M25297)			
Fwd	GCTGCTTTGGGCAGAAGATAGA (SEQ ID NO: 22)	350-371	Rat
Probe	CCTCAGCCCGTCACAGCCCAA (SEQ ID NO: 23)	394-414	
Rev	GCCAGGAGGTCTTCCTAAAACA (SEQ ID NO: 24)	416-437	

The probes were labelled at the 5' and 3' positions with 6-carboxyfluorescein reporter and 6-carboxytetramethylrhodamine quencher, respectively. The position of the primers and probes were annotated according to the sequences derived from GenBank (accession numbers given in parenthesis). Fwd, forward; Rev, reverse.

Replacement Paragraph for page 35, line 15 to line 35

Table 3. Sequences for semi-quantitative PCR and real-time quantitative RT-PCR primers and probes of candidate gene transcripts

Gene/primer	Sequence (5'→3')	Species
Cyclophilin A (NM_021130)		
Fwd	TGCTGGACCCAACACAAATG (SEQ ID NO: 25)	
Probe	TTCCCAGTTTTTCATCTGCACTGCCA (SEQ ID NO: 26)	Human
Rev	TGCCATCCAACCACTCAGTC (SEQ ID NO: 27)	
Galectin-3 (NM_002306)		
Fwd	CTCGCATGCTGATAACAATTCTG (SEQ ID NO: 28)	
Probe	CGGTGAAGCCCAATGCAAACAGAATT (SEQ ID NO: 29)	Human
Rev	GCAACATCATTCCCTCTTTGG (SEQ ID NO: 30)	
MCP-1 (M57441)		
Fwd	GCAGGTCTCTGTCACGCTTCT (SEQ ID NO: 31)	
Rev	GATGATCCCAATGAGTCGGCT (SEQ ID NO: 32)	Rat

The probes were labelled at the 5' and 3' positions with 6-carboxyfluorescein reporter and 6-carboxytetramethylrhodamine quencher, respectively. The position of the primers and probes were annotated according to the sequences derived from GenBank (accession numbers given in parenthesis). Fwd, forward; Rev, reverse.